Claims

1 A method of detecting an activity of an antibiotic, in a sample, the method comprising the steps of:
(a) providing a microorganism in which a first endogenous gene encoding peptidyltransferase activity is inactivated, which activity is necessary for growth of the microorganism, and which activity can be complemented by a second, different, peptidyltransferase, which second peptidyltransferase is inducible in the microorganism by the presence of the antibiotic,
(b) contacting the sample with the microorganism,
(c) observing the microorganism for growth,
wherein growth of the microorganism is correlated with the presence of the antibiotic.

2 A method as claimed in claim 1 wherein the antibiotic is a glycopeptide antibiotic which interferes with the physical integrity of the cell envelope.

3 A method as claimed in claim 1 or claim 2 wherein second peptidyltransferase is endogenous

4 A method as claimed in any one of the preceding claims wherein the peptidyltransferase activity is nonribosomal and operates on a substrate in the cell involved in cross-bridge formation of the microorganism cell wall.

5 A method as claimed in claim 4 wherein the peptidyltransferase activity adds a single glycine to a stem pentapeptide substrate which can form a cross-bridge through D-ala transpeptidation.

6 A method as claimed in claim 5 wherein the first peptidyltransferase acts on a stem pentapeptide substrate which terminates D-ala-D-ala

7 A method as claimed in claim 6 wherein the first endogenous gene encoding peptidyltransferase activity is *femX* (SCO3904).

8 A method as claimed in any one of claims 5 to 7 wherein the second peptidyltransferase acts on a stem pentapeptide substrate which terminates D-ala-D-lac

9 A method as claimed in claim 8 wherein the second peptidyltransferase is encoded by *vanF* (SCO3593).

10 A method as claimed in any one of claims 5 to 9 wherein the presence of the antiobiotic in the sample induces additional enzymes which modify stem pentapeptide cell wall precursors such as to provide a substrate for the second peptidyltransferase.

11 A method as claimed in claim 10 wherein the additional enzymes may be present in the same genomic cluster as the second peptidyltransferase.

12 A method as claimed in claim 10 wherein the additional enzymes are VanHAX enzymes encoded by *vanH* (SCO3594); *vanA* (SCO3595); *vanX* (SCO3596).

13 A method as claimed in any one of the preceding claims wherein the bacterium is an actinomycete

14 A method as claimed in claim 13 wherein the bacterium is *Streptomyces.*

15 A method as claimed in claim 14 wherein the bacterium is *Streptomyces coelicolor*

16 A method as claimed in claim 15 wherein the bacterium is *Streptomyces coelicolor* A3(2).

17 A method as claimed in any one of claims 2 to 16 wherein the microorganism is a strain in which enzymes which may otherwise degrade glycopeptidic antibiotics have been inactivated.

18 A method as claimed in any one of the preceding claims wherein the sample is selected from: a culture supernatant; a soil

isolate; the product of combinatorial chemical synthesis; the product of combinatorial biosynthesis.

19 A method as claimed in any one of the preceding claims wherein the activity is qualitatively correlated with the presence or absence of an antibiotic.

20 A method as claimed in any one of the preceding claims wherein the activity of the sample is further screened for antibiosis of a target organism.

21 A process of producing a microorganism for use in a method of any one of the preceding claims, which process comprises inactivating in the microorganism a first endogenous gene encoding peptidyltransferase activity,

wherein said activity is necessary for growth of the microorganism,

and wherein said activity can be substituted by a second, different, peptidyltransferase, which second peptidyltransferase is inducible in the microorganism by the presence of an antibiotic.

22 A process as claimed in claim 21 wherein the first endogenous gene encoding peptidyltransferase activity is inactivated by introducing therein a heterologous marker sequence.

23 A process as claimed in claim 21 or claim 22 wherein second peptidyltransferase is endogenous

24 A process as claimed in claim 21 or claim 22 wherein the microorganism is transformed with a gene encoding the second peptidyltransferase

25 A process of producing an isolated antibiotic which affects cell integrity, which method comprises the steps of:
(a) performing a method according to any one of claims 1 to 20 such as to identify the activity of the antibiotic in a sample,
(b) isolating the antibiotic from the sample.

26 A process as claimed in claim 25 which is preceded by the

step of providing a transformed microorganism according to the process of any one of claims 21 to 24.

27 A microorganism for use in a method of any one of claims 1 to 20, which microorganism is characterised in that it includes

a first endogenous gene encoding peptidyltransferase activity which is inactivated, which activity is necessary for growth of the microorganism, and which activity can be substituted by

a second, different, peptidyltransferase, which second peptidyltransferase is inducible in the microorganism by the presence of the antibiotic.

28 A system for detecting an activity of an antibiotic in a sample comprising:

(a) the transformed microorganism of claim 27,

(b) means for detecting the viability of the microorganism in the presence of the antibiotic.

29 A kit for performing a method according to any one of claims 1 to 20, which kit comprises a preparation of the microorganism of claim 27, plus further means for carrying out the contact or observation steps.